PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference WA/46538	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/05896	International filing date *(day/month/year)* 05.06.2003	Priority date *(day/month/year)* 05.06.2002
International Patent Classification (IPC) or both national classification and IPC C07K16/02		
Applicant WALCOM ANIMAL SCIENCE (I.P.4) LIMITED		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 8 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
05.01.2004	23.07.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer van Heusden, M Telephone No. +49 89 2399-8145

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/05896

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-38 as originally filed

Claims, Numbers

1-43 received on 02.07.2004 with letter of 02.07.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-43
	No:	Claims	
Inventive step (IS)	Yes:	Claims	18-20, 22, 24-42
	No:	Claims	1-17, 21, 23, 43
Industrial applicability (IA)	Yes:	Claims	1-23, 36
	No:	Claims	24-35, 37-43 (?)

2. Citations and explanations

see separate sheet

Additional remarks to section V:

1. Novelty and Inventive step (Article 33(2) and (3) PCT)

1.1 The present application discloses a method of producing antibodies, by preparing an antigen from the adipose tissues of a source animal, producing antibodies to said antigen in an egg-laying animal, the latter belonging to a different species than the source animal. It further relates to the resulting antibodies and their medical applications. It also relates to a feed additive or a medicament comprising said antibodies. Finally it relates to methods of modulating adipose content of a target animal using said antibodies.

1.2 The documents mentioned in this report are numbered as in the International Search Report (ISR), i.e. D1 corresponds to the first document of the ISR etc.

1.3 The present application does not seem to satisfy the criterion set forth in Article 33(3) PCT because the subject matter of claims 1-17, 21, 23 and 43 does not appear to involve an inventive step in view of documents D1-D5.

The subject matter of claims 1 and 43 relates to a method of producing antibodies using antigen from adipose tissue of a source animal and making antibodies in an egg-laying animal that is different from the source animal. The fact that the antibodies so produced cross react with adipose tissue from a further (target) species different from the source species is a result that is achieved (inherently) which does not constitute a technical feature characterizing the method.

The closest prior art to evaluate the inventiveness of claims 1 and 43 is any of documents D3-D5, which all disclose the production of antibodies against adipocyte, plasma membranes of adipocyte, or antigens thereof. The antibodies are produced in sheep (D3, D5) or rabbit (D4). The subject matter of claims 1 and 43 differs from said prior art documents in that the antibodies are produced in an egg-laying animal. It is, however, well known in the art that egg-laying animals, for instance chickens, are a suitable host for large scale antibody production and purification. This is also apparent from document D1, wherein antibodies against chicken adipocyte membranes are prepared in chicken (paragraphs 40-45), and from D2, wherein antibodies against CCK are produced in chicken (example 1). It follows that the production of antibodies against adipose tissue in an egg- laying animal does not involve an inventive step (claims 1-14). It follows that the antibodies resulting from the method of claims 1-14 (antibody according to claims 15-17)

and a medicament comprising said antibodies (claims 21 and 23) cannot be considered inventive either.

1.4 The applicant has argued that the inventive concept of claim 1 lies in the fact that antibodies against adipose tissue antigen from one species can cross-react with antigen of adipose tissue of a closely related/different species. As indicated above, this feature does not constitute a technical feature characterizing the method of claim 1, but rather relates to an intended use. It is anticipated that in the case that claim 1 were to be limited to a method as defined in claim 1 and further comprising the step of administering the resulting antibodies to a target animal belonging to a closely related species, said method would be objected to for insufficient disclosure. The applicant has argued that the skilled person would not have a reasonable expectation of success in finding cross-reactivity between adipose tissue antigens of different species. The applicant has shown that such cross-reactivity exists between pig adipose tissue antigen and rat adipose tissue antigen, using antibodies made in chicken. Therefore an inventive step could at most be recognized for a method based on the specific cross-reactivity of antibody, made in chicken, against adipose tissue antigen of pig and rat.

1.5 None of the cited prior art documents suggests that an antibody against adipose tissue antigen can be effective in modulating adipose tissue fat content of a target animal when administered orally. This implies that the antibodies are effective even after passing the intestinal barrier. Thus an inventive step can be recognized for a method of modulating content of adipose tissue in a target animal comprising the oral administration of antibody against adipose tissue antigen (claims 24-42). Therefore also feed additive comprising said antibody (claims 18-20) can be considered inventive. The same is true for a medicament comprising said antibody and being adapted to be administered via ingestion (claim 22).

2. Industrial applicability (Article 33(4) PCT)

2.1 The subject matter of claims 1-23 and 36 appears to be industrially applicable.

2.2 The subject matter of claims 24-35 and 37-43 includes methods of treatment of the human or animal body and is thus excluded from examination by Article 34(4)(a)(i) PCT in combination with Rule 67(iv) PCT. For the assessment of these claims on the question

whether they are industrially applicable, no unified criteria exist in PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject matter of claims to the use of a compound in medical treatment, but will allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

The applicant is already informed that in the case of a European application, claims 24-35 and 37-43 do not seem to be allowable because 'methods of treatment of human or animal body by surgery or by therapy and diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application'.

Furthermore the applicants attention is drawn to the discrepancy between claim 1 ("non-therapeutic method") and claim 11 ("patient").

Claims:-

1. A non-therapeutic method of producing antibodies that bind adipose tissues in a target animal in need of said antibodies for modulating the content of adipose tissues in said target animal, the method comprising the steps of:

(i) preparing an antigen from adipose tissues of a source animal wherein said source animal and said target animal belong to closely related species;

(ii) administering said antigen to an egg laying animal to cause production of said antibodies wherein said egg-laying animal and said target animal belong to different species; and

(iii) obtaining said antibodies from eggs of said egg-laying animal wherein said egg-laying animal and said source animal belong to different species.

2. A method according to Claim 1 comprising a step of causing production of said antibodies from within the body of said egg-laying animal.

3. A method according to Claim 1 or 2 comprising a step of causing deposition of said antibodies to said eggs of said egg-laying animal.

4. A method according to any preceding claim wherein said step of obtaining comprises a step of isolating said antibodies from the egg yolk of said eggs.

5. A method according to any preceding claim wherein said antigen comprises plasma membrane, its adipocyte plasma membrane surface proteins, or fragments thereof, of said adipose tissues of said source animal.

6. A method according to any preceding claim wherein said antibodies are polyclonal antibodies.

7. A method according to any preceding claim wherein said source animal and said egg-laying animal belong to distinctly different species.

8. A method according to any preceding claim wherein said target animal and said egg-laying animal belong to distinctly different species.

9. A method according to any preceding claim wherein said target animal is a farm animal.

10. A method according to any preceding claim wherein said source animal and/or said target is a swine.

11. A method according to any one of Claims 1 to 8 wherein said target animal is a patient.

12. A method according to any preceding claim wherein said egg-laying animal in an avian animal and said source animal is a non-avian animal.

13. A method according to any preceding claim wherein said source animal is a mammal.

14. A method according to any preceding claim wherein one or more of said animals is sacrificed after said method.

15. Antibodies obtainable according to the method defined in any one of Claims 1 to 14.

16. Antibodies according to Claim 15 for use in a method of treatment or diagnosis.

17. Use of antibodies defined in Claim 15 or 16 for the manufacture of a medicament for the treatment of a condition caused by an excess of adipocytes.

18. A feed additive comprising an effective amount of antibodies defined in Claim 15 or 16.

19. A feed additive according to Claim 18 adapted to lower the content of said adipose tissues in said target animal.

20. A feed additive according to Claim 18 or 19 wherein said composition comprises egg yolk of said eggs containing said antibodies.

21. A medicament comprising a pharmaceutically effective amount of antibodies defined in Claim 15 or 16.

22. A medicament according to Claim 21 adapted to be administered via ingestion.

23. A medicament according to Claim 21 adapted to be administered via injection.

24. A method of modulating content of adipose tissues in the body of a target animal in need of antibodies, comprising the steps of:

(i) preparing an antigen from adipose tissues of a source animal;

(ii) administering said antigen to an egg-laying animal;

(iii) allowing said antibodies to be produced by said egg-laying animal in response to said antigen;

(iv) obtaining said antibodies from eggs of said egg-laying animal; and

(v) administering a pharmaceutically effective amount of said antibodies to said target animal by ingestion, wherein said source animal and said egg-laying animal belong to different species.

25. A method according to Claim 24 wherein said step of obtaining comprises a step of isolating said antibodies from the egg yolk of said eggs.

26. A method according to Claim 24 or 25 comprising a step of binding said antibodies to characterizing components of plasma membrane of said adipose tissues in said target animal.

27. A method according to Claim 24, 25 or 26 comprising a step of binding said antibodies to granular viscosity proteins of said adipose tissues in said target animal.

28. A method according to Claim 24, 25 or 26 comprising a step of binding said antibodies to fiber viscosity proteins of said adipose tissues in said target animal.

29. A method according to any one of Claims 24 to 28 wherein said antigen comprises plasma membrane, its adipocyte plasma membrane surface proteins, or fragments thereof, of said adipose tissues of said source animal.

30. A method according to any one of Claims 24 to 29 wherein said antibodies are polyclonal antibodies.

31. A method according to any one of Claims 24 to 30 wherein said source animal and said egg-laying animal belong to distinctly different species.

32. A method according to any one of Claims 24 to 31 wherein said target animal and said egg-laying animal belong to different species.

33. A method according to Claim 32 wherein said target animal and said egg-laying animal belong to distinctly different species.

34. A method according to any one Claims 24 to 33 wherein said target animal and said source animal belong to a same species.

35. A method according to any one Claims 24 to 33 wherein said target animal and said source animal belong to a closely related species.

36. A method according any one of Claims 24 to 36 wherein said method is a non-therapeutic method.

37. A method according to any one of Claims 24 to 36 wherein said target animal is a farm animal.

38. A method according to any one of Claims 24 to 37 wherein said source animal and/or said target is a swine.

39. A method according to any one of Claims 24 to 36 wherein said target animal is a patient.

40. A method according to any one of Claims 24 to 39 wherein said egg-laying animal in an avian animal and said source animal is a non-avian animal.

41. A method according to any one of Claims 24 to 40 wherein said source animal is a mammal.

42. A method according to any one of Claims 24 to 41 wherein one or more of said animals is sacrificed after said method.

43. A method of producing antibodies that bind adipose tissues in a target animal in need of said antibodies for modulating the content of adipose tissues in said target animal, the method comprising the steps of:

(i) preparing an antigen from adipose tissues of a source animal wherein said source animal and said target animal belong to closely related species;

(ii) administering said antigen to an egg-laying animal to cause production of said antibodies wherein said egg-laying animal and said target animal belong to different species; and

(iii) obtaining said antibodies from eggs of said egg-laying animal wherein said egg-laying animal and said source animal belong to different species.